REMARKS

Claims 1, 9, 10, 17, and 27 have been amended herein. Claim 8 has been canceled herein. Such cancellation is without prejudice on the merits to prosecution of this claim in one or more continuing applications.

Claims 1-27 remain in the case. Favorable reconsideration is respectfully requested.

Applicants thank Examiner Riley for indicating that Claims 21-27 have been allowed. Claim 27 has been amended herein solely to correct a discrepancy in the preamble. As originally filed, Claim 27 read "The array of Claim 21...." Claim 21 actually recites a method. Claim 27 has therefore been amended accordingly to recite a method, rather than an array.

The following remarks address the issues presented in the Office Action in the order of their appearance.

Rejection of Claims 1, 2, 4, and 7 Under 35 USC §102(b) Over Jordan et al. (1997) *Anal. Chem* 69:4939-4947:

This rejection has been overcome by inserting the subject matter of now-cancelled Claim 8 into Claim 1 as amended. Claim 8 was not made subject to this rejection. Thus, by amending Claim 1 to include the subject matter of Claim 8, Applicants respectfully submit that this rejection has been overcome.

Applicants therefore request that the rejection of Claims 1, 2, 4, and 7 under 35 USC §102(b) over Jordan et al. be withdrawn.

Rejection of Claims 1, 2, 4, and 7 Under 35 USC §102(b) Over Thiel et al. (1997) *Anal. Chem* 69:4948-4956:

This rejection has been overcome by inserting the subject matter of now-cancelled Claim 8 into Claim 1 as amended. Because Claim 8 was not made subject to this rejection, by amending Claim 1 to include the subject matter of Claim 8, Applicants respectfully submit that this rejection has been overcome.

Applicants therefore request that the rejection of Claims 1, 2, 4, and 7 under 35 USC §102(b) over Thiel et al. be withdrawn.

Rejection of Claims 1-20 Under §103(a) Over Jordan et al. or Thiel et al. in View of Linsley et al., U.S. Patent No. 6,232,068:

This rejection is traversed on two grounds: 1) because the Linsley et al. patent is totally silent with regard to detecting nucleic acids via surface plasmon resonance (SPR), there is no motivation to combine the Linsley et al. patent (which is totally silent with regard to SPR) with the Jordan et al. and Thiel et al. papers; and 2) even when the combination is made, the **combined** teaching of the references, taken alone or in any combination, fails to teach or suggest the present invention.

Taking these two points in reverse order, this rejection is respectfully traversed because the combination of Jordan et al. with Linsley et al., as well as the combination of Thiel et al. with Linsley et al. fails to teach or suggest a method that uses an SPR-capable array on which is immobilized nucleic acid probes that are "species- or taxon-specific" (a positive requirement of Claim 1) or nucleic acid probes that are "specifically reactive with mRNA or cDNA corresponding to a gene of interest" (a positive requirement of Claim 11).

In this regard, note that both of the primary references (Jordan et al. and Thiel et al.) describe SPR experiments that use arbitrary matched pairs of oligos, and were performed under tightly-controlled experimental conditions. In short, in both of these references, the probes that are immobilized on the SPR substrate are arbitrary synthetic oligonucleotides that were then exposed to highly purified, perfectly complementary sequences contained in a solution devoid of any potentially interfering nucleic acid sequences. Thus, there is no reasonable likelihood of success, based upon either of these two references, that the conditions described in the references can be implemented using species-specific, taxon-specific, mRNA-specific, or cDNA-specific immobilized probes to detect a complementary oligonucleotide from a complex mixture.

For example, see Table 1 of the Jordan et al. paper (at page 4943). Table 1

presents the various oligonucleotides that are disclosed and discussed in the Jordan et al. paper. All of the immobilized oligos (designated P1, P2, and P4 in Table 1) are synthetic. Likewise, all of their respective complementary sequences (BC1, BC2, and C4a in Table 1) are also synthetic oligos and are perfect matches for their immobilized counterparts. See also the materials section of Jordan et al., which states that all of the oligos, both the immobilized oligos and the complementary oligos in solution, were fabricated from scratch and then purified by reversed-phase binary gradient elution HPLC prior to use.

Of critical importance to the present claims is that none of the immobilized oligos disclosed in the Jordan et al. reference are species-specific, taxon-specific, mRNA-specific, or cDNA-specific. The specificity of the oligos immobilized on the SPR surface is a positive requirement of both Claim 1 and Claim 11, the two independent claims subject to this rejection.

Thiel et al. also uses arbitrary sequences that are not species-specific, taxon-specific, mRNA-specific, or cDNA-specific. See Table 1 of Thiel et al. at page 4950. "Probes I, II, and III" are the immobilized oligos used in the study described by Thiel et al., and "Targets IV, V, and VI" are the oligos in solution. As in the Jordan et al. paper, Thiel et al. synthesized all of the oligonucleotides from scratch (see page 4950, right-hand column, under the "Experimental Section.") All of the sequences of the oligonucleotides used by Thiel et al. are thus completely arbitrary in nature. None of the oligos described by Thiel et al. are species-specific, taxon-specific, mRNA-specific, or cDNA-specific, a specificity that is required by the present claims.

Thus, the **combined** teaching of the Jordan et al. and Thiel et al. references fails to disclose or suggest species-specific, taxon-specific, mRNA-specific, or cDNA-specific probes immobilized on an SPR-capable substrate. This particular specificity of immobilized oligos is a positive requirement of both Claim 1 and Claim 11, the two independent claims subject to this rejection.

Combining either or both of the Jordan et al. or Thiel et al. references with the Linsley et al. patent does not cure the shortcomings of the two primary references because the Linsley et al. patent is completely and totally silent with regarding to

detecting nucleic acid hybridization using SPR. Thus, the combination of Jordan et al., Thiel et al, and Linsley et al. sheds nor more light on the claimed invention than the Jordan/Thiel combination because the Linsley et al. patent neither mentions SPR nor suggests its use. In short, the Linsley et al. patent is wholly unrelated and irrelevant to the present invention.

The protocol described in the Linsley patent is explicitly directed to the detection of RNA in general and total cellular RNA in particular. The fundamental basis of the Linsley et al. protocol is to immobilize DNA onto a solid surface (not an SPR-capable surface), and then contact the immobilized DNA with RNA in solution to yield RNA/DNA heteroduplexes. See Linsley et al. at, for example, column 5, line 45, to column 6, line 4. Of critical importance to the present claims is that the only means described by Linsley et al. to detect the RNA./DNA heteroduplexes is to contact the heteroduplexes with "anti-heteronucleic acid" antibodies. (Id.)

It is this type of labor intensive, label-dependent detection that the present invention explicitly avoids. See the present specification, for example, at page 6, first paragraph. By using SPR as a method for detecting nucleic acid hybridization, no labeling of the nucleic acid is required. Thus, the present invention can detect sequence-specific hybridization without using fluorophores or antibodies for detection.

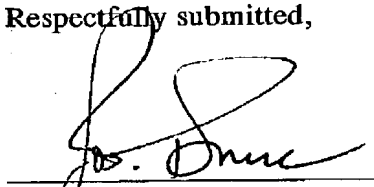
Thus, Applicants also traverse this rejection because there is no motivation for combining the Jordan et al. or Thiel et al. references with the Linsley et al. patent in the first instance. Linsley is totally, wholly, and completely silent with regard to detecting nucleic acid hybridization via surface plasmon resonance. Therefore, armed with the information provided in the primary references to Jordan et al. and Thiel et al., a skilled artisan would not look to the Linsley et al. patent, which is directed to a totally unrelated protocol that requires enzymatic detection.

For these reasons, Applicants submit that the rejection of Claims 1-20 under §103(a) over Jordan et al. or Thiel et al. in view of Linsley et al. is improper. Withdrawal of the same is respectfully requested.

CONCLUSION

Applicants submit that the application is now in condition for allowance. Early notification of such action is earnestly solicited.

Respectfully submitted,



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